IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Application No. : **10/680,742**

Applicants : **James E. Hagstrom et al.**

Filed : **01/06/2003**

Art Unit : **1632**

Examiner : **David Montanari**

Docket No. : **Mirus.013.03.8**

For: **Processes for Delivery of Polynucleotides to the Prostate**

Commissioner of Patents
PO Box 1450
Alexandria, VA 22313-1450

AMENDED APPELLANT'S BRIEF

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i. Real party in interest:

The real parties in interest are: James E. Hagstrom, Mark Noble, Julia Hegge, Vladimir G. Budker; and, by assignment, Mirus Corporation, which has changed its name to MirusBio Corporation, incorporated under the laws of the State of Delaware and located at 505 South Rosa Road, Madison, WI 53719.

ii. Related appeals and interferences:

There are no interferences known to appellant, the appellant's legal representative, or assignee which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

iii. Status of Claims:

Claims 1-2 and 4-14 have been rejected and are hereby appealed.
Claims 3 and 15-20 have been canceled.

iv. Status of amendments:

An amendment was filed subsequent to the date of the final rejection. The amendment was not entered.

v. Summary of claimed subject matter for independent claim 1:

A needle, catheter, or similar device is used to inject a solution containing a polynucleotide into a particular vessel. The vessel is chosen by selecting an afferent or efferent vessel of the prostate tissue. The injection can be performed using a needle that traverses the skin of the mammal and enters the lumen of a vessel. Alternatively, a catheter can be inserted at a distant site and threaded through a vessel(s) such that the instillation port of the catheter resides in a vessel that more directly connects with the prostate tissue. Balloon catheters allow for occlusion of the vessel as well as insertion of a solution into the vessel. The instillation port of a balloon catheter is located between the balloon and the prostate tissue. (Specification: page 5, line 37 to page 6, line 17)

Injecting into a vessel an appropriate volume at an appropriate rate increases permeability of the vessel and increases the volume of extravascular fluid in the prostate tissue. Permeability of vessel walls and volume of extravascular fluid can be further increased by occluding outflow of fluid-both bodily fluid and injection solution-from the tissue or local vascular network. For example, a solution can be injected into an afferent vessel supplying the prostate while afferent vessels(s) of the prostate, efferent vessel(s) of the prostate or both, are transiently occluded. Branching or collateral vessels or tributaries may also be occluded. Natural occlusions may be taken advantage of for impeding fluid outflow from the target vasculature. (Specification: page 7, lines 1-15)

Permeability of a vessel is the propensity for macromolecules to move out of a vessel and enter the extravascular space. One measure of permeability is the rate at which macromolecules move through the vessel wall and out of the vessel. Another measure of permeability is the lack of force that resists the movement of fluid or macromolecules through the vessel wall and out of the vessel. The choice of injection volume and rate are dependent upon: the size of the animal, the size of the vessel into with the solution is injected, the size and or volume of the prostate, the bed volume of the prostate vasculature, and the nature of the prostate or vessels supplying the prostate. (Specification: page 7, lines 17-30)

For a given mammal, the volume and rate identified as effective for delivery to prostate in one mammal can generally be considered to be effective for delivery to prostate in other mammals. (Specification: page 9, lines 29-31)

Applicants have provided numerous examples using the described process for delivering and expressing polynucleotides in extravascular mammalian prostate tissue.

vi. Grounds of rejection to be reviewed on appeal:

Whether claims 1-2, and 4-14 are unpatentable under 35 U.S.C. 112, for failing to comply with the enablement requirement.

vii. Argument:

Rejection of the Claims under 35 U.S.C. 112:

Rejection of claims 1-2, and 4-14 under §112 for failing to comply with the enablement requirement on page 2 of the Action.

On pages 2 and 3 of the Office Action the Examiner states that the claimed process encompasses gene therapy. Further stating that thought the claimed process may envision other uses, gene therapy is one of these, and thus is not fully enabled. The examiner refers to the previous Office Action for the detail of how the claimed process encompasses gene therapy.

In the previous Office Action on page 7 and 8 the Examiner states: "The breadth of the claims encompasses delivering a polynucleotide to a prostate cell in any mammal. This embodiment reads on gene therapy because the claimed process results in the expression of an exogenous polynucleotide in a target mammal even though no treatment is specified in the base claim of the instant application. The specification provides that the **only intended use** of the claimed invention is a method of gene therapy to treat disease, specifically, prostate cancer."

Beginning with "the only intended use" assertion of the Examiner, Applicants provided other expressly stated uses in their subsequent response. Specifically, "The specification states on page 1 lines 25-27, 'Delivery of genes to prostate in animal models will also further biomedical research into the causes, mechanisms and potential treatments of enlarged prostate, prostate cancer and benign prostatichyperplasia.' On page 2 lines 12-13, the specification states, 'In a preferred embodiment, the present invention provides processes for in vivo delivery of polynucleotides to prostate cells in a mammal.' On page 3 lines 29-30 and 33-34, the specification states, 'In a preferred embodiment, the described processes can be used to deliver a polynucleotide to a prostate cell for the purpose of altering the endogenous properties of the cell and alternatively, the polynucleotide may be delivered to the cell to facilitate pharmaceutical drug discovery, drug target validation or for research.' Finally, the specification states, on page 12 lines 15-19, 'The polynucleotide can be a sequence whose presence or expression in a cell alters the expression or function of cellular genes or RNA. A polynucleotide can be delivered to a cell to express an exogenous nucleotide sequence, to inhibit, eliminate, augment, or alter expression of an endogenous nucleotide sequence, or to affect a specific physiological characteristic not associated with the cell prior to delivery of the polynucleotide.' These quotations from the specification fully support utilities for delivery of polynucleotides for purposes other that gene therapy to treat disease.

However, the Examiner's response in the current Action is "though the claimed process may envision other uses" which is a contradiction, without explanation, to his previous statement iterating that gene therapy was the "only intended use." When an Examiner rejects a claim based on some type of reasoning, he cannot dismiss his former reasoning without explanation, as he does in the current Action.

Applicants have claimed a process of delivery and expression in mammals and no more. They have supported the claims with numerous examples in the specification showing delivery and expression to mice, rats and monkeys. Applicants do not have to prove that a correlation exists between a particular activity and an asserted therapeutic use [or in this case a non-asserted therapeutic use] of a compound as a matter of statistical certainty, nor do they have to provide actual evidence of success in treating humans where such a utility is asserted. Instead, as the courts have repeatedly held, all that is required is a reasonable correlation between the activity and the asserted use. Nelson v. Bowler, 626 F.2d 853, 857, 206 USPQ 881, 884 (CCPA 1980).

Applicants have not claimed a gene therapy. The Examiner has stated, on his own, that Applicants have claimed a gene therapy. The term is very broad and Applicants' process certainly could be used in research toward a therapy or as a part of a therapeutic treatment developed by another. In either event, Applicants' process is enabled and only reasonable adjustments to volume and pressure need be made for the process of delivering and expressing DNA to be applicable to any mammal.

viii. Claims Appendix:

1. (previously presented) A process for delivering DNA to a prostate cell in a mammal comprising:

    a) inserting a delivery device into a lumen of an afferent or efferent vessel of the prostate;

    b) injecting a solution containing the DNA into the lumen of the vessel;

    c) increasing permeability of the vessel to the DNA;

    d) delivering the DNA to the prostate cell outside of the vessel; and,

    e) expressing the DNA.

2. (original) The process of claim 1wherein fluid flow out of the prostate tissue is impeded by occlusion of at least one vessel.

immune response.

3. (canceled)

4. (original) The process of claim 1wherein the vessel consists of a blood vessel.

5. (original) The process of claim4 wherein the blood vessel consists of a vein.

6. (original) The process of claim4 wherein the blood vessel consists of an artery.

7. (previously presented) The process of claim5 wherein the vein is selected from the list consisting of prostatic venous plexus, prostatic vein, tributaries of the deep dorsal vein of the penis, dorsal vein of the penis, internal iliac vein, and vesical venous plexus, and their tributaries.

8. (original) The process of claim 6 wherein the artery is selected from the list consisting of: inferior vesical artery, internal iliac artery, prostatic artery, internal pudic artery, hemorrhoidal artery, and rectal artery, and their tributaries.

9. (previously presented) The process of claim1wherein expression of the DNA induces an immune response.

10. (previously presented) The process of claim 1 wherein the DNA is associated with a transfection agent.

11. (original) The process of claim1 wherein the solution contains a compound that increases vascular permeability.

12. (previously presented) The process of claim 1 wherein expression of the DNA alters the endogenous properties of the cell.

13. (original) The process of claim 1wherein the mammal has benign prostatic hyperplasia.

14. (original) The process of claim 1wherein the mammal has prostate cancer.

15.-20. (canceled)

IX. Evidence appendix:

None

x. Related proceedings appendix:
None

Pages 1-14 are respectfully submitted,
/Mark K Johnson/
Mark K. Johnson Reg. No. 35,909
Mirus Bio Corporation
505 South Rosa Road
Madison, WI 53719
608-238-4400

I hereby certify that this correspondence is being transmitted to the USPTO addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450 on this date: February 28, 2007.

/Mark K Johnson/
Mark K Johnson